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# Investigation of Medication Adherence and Rejection in Liver Transplant for Cystic Fibrosis (CF)

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(\* ) indicates primary project advisor



# Introduction

- Upwards of 40% of transplant recipients are non-adherent to their medications<sup>3</sup>
- More specifically, CF patients are more than 50% non-adherent to treatment regimens<sup>5</sup>
- Non-adherence often results in rejection, and therefore can diminish the long-term survival and outcomes of transplantation<sup>4</sup>
- Despite high non-adherence rates, post-liver transplant graft survival of CF patients is comparable to that for other indications of pediatric liver transplantation<sup>1</sup>
- Patient survival after liver transplantation for CF patients was lower, but mortality was not attributed to graft failure<sup>2</sup>



# Introduction

- Non-adherence is high in the CF population
  - Non-adherence is best estimated by the Medication Level Variability Index (MLVI)
- Graft loss from rejection is not increased
- We sought to examine the relationship between adherence and rejection in the CF population

# Objectives & Hypothesis

- Research Question
  - Is there a difference between adherence, measured by Medication Level Variability Index (MLVI), and biopsy proven graft rejection rates in pediatric liver transplant recipients with CF compared to those without CF ?
- Hypothesis
  - We hypothesize that MLVI is higher and rejection rates are lower in subjects with CF

# Approach & Results

- Study design: Retrospective medical chart review
- Population: 9 pediatric CF liver transplant recipients
- Comparison Group: 9 non-CF pediatric liver transplant recipients
- Outcome: Medication adherence measured by Medication Level Variability Index (MLVI) and liver biopsy-proven graft rejection
- Data source and collection: EPIC medical records from Children's Hospital of Philadelphia patients between 1995 and 2018 to find medication levels (MLVI) and liver biopsy results (when relevant)
- Rationale: A retrospective chart review was most appropriate given the sample size and measured outcomes

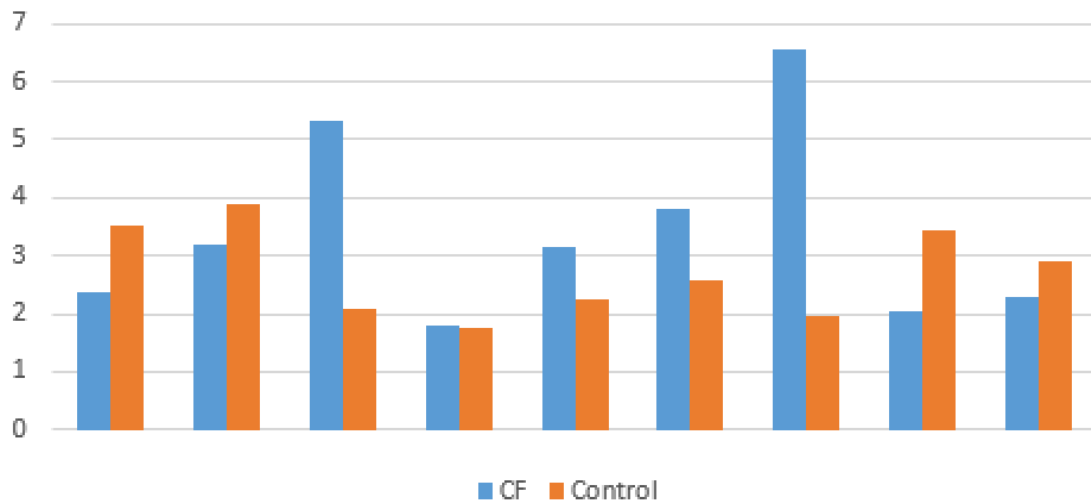
# Approach & Results

- Analysis: An unpaired t-test was performed to determine if there was a difference in MLVI between the two groups, and liver biopsy reports were used to determine rates of rejection
- Findings:
  - There was a trend for higher MLVI in the CF group, however, this did not reach statistical significance comparing MLVI for the CF group (M=3.40; SD= 1.60) and non-CF group (M=2.71; SD= 0.77);  $t(16)=1.15$ ;  $p=0.26$
  - 2 subjects in the CF group (22%) and 3 subjects (33%) in the non-CF group had rejection on liver biopsy
  - When comparing rates of biopsy-proven rejection in CF and controls with MLVI >2 , 14% of those with rejection were CF subjects and 13% were control subjects

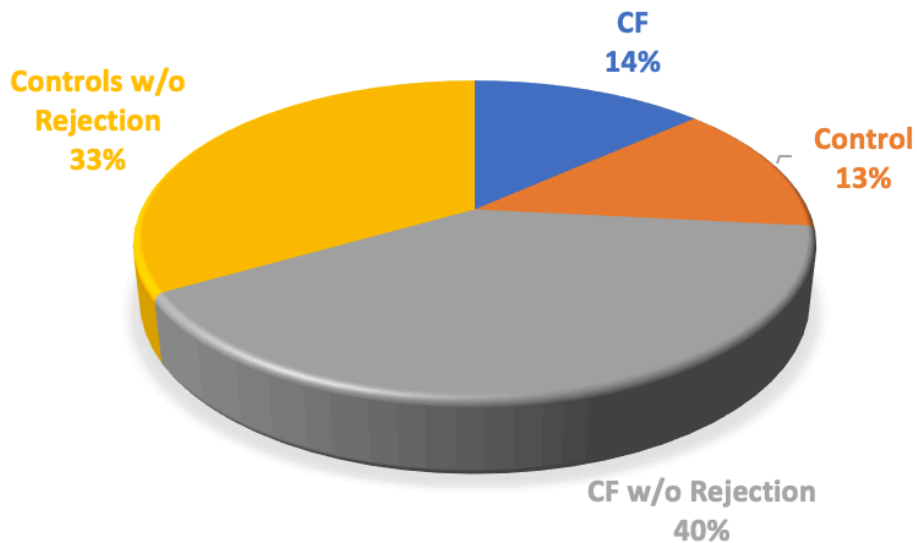


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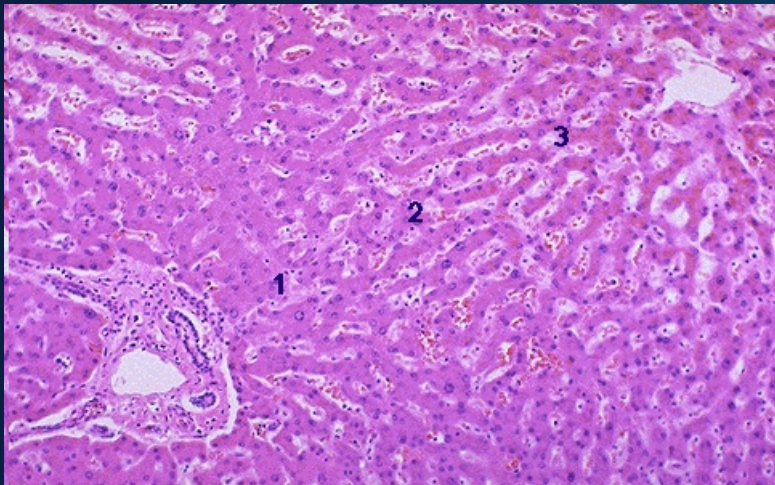
### MLVI Comparison Between CF Subjects and their Matched Controls



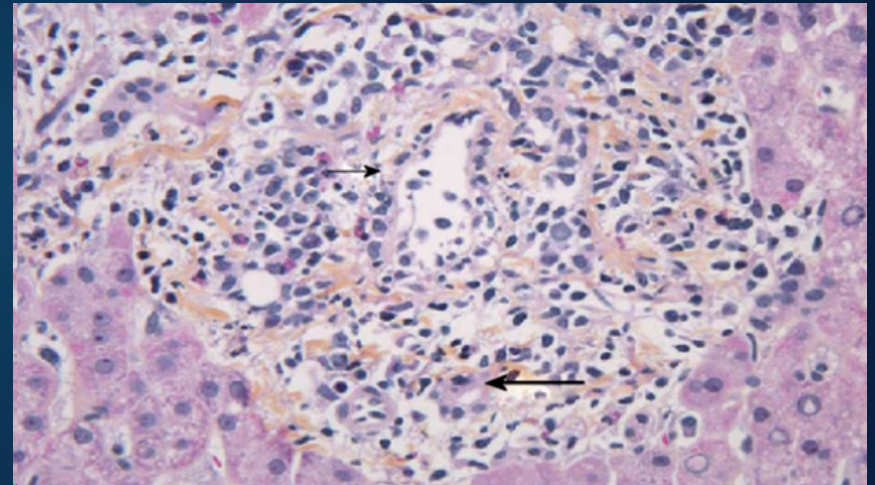
### COMPARING RATES OF BIOPSY PROVEN REJECTION BETWEEN CF AND CONTROLS WITH MLVI >2







A. Normal portal tract and central vein with zones of the hepatic lobule labeled



B. Portal tract with features of rejection including mixed lymphocytic and eosinophilic infiltrate of a portal vein (small arrow) and damaged bile duct (large arrow)



# Conclusions

- These results show adherence to immunosuppressive medications (as reflected by MLVI) and rates of biopsy-proven rejection are not statistically different between CF and non-CF liver transplant recipients
- Small sample size limits the strength of this study
- MLVI has been associated with increased rate of rejection, however the CF population may differ from this expectation due immune activity from chronic lung inflammation and is worthy of further study



# Future Directions

- Further study with a multi-center cohort may reveal important differences in rejection risks in CF
- Furthermore, study on socioeconomic factors that may influence medication adherence and rejection rates is needed

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